

other localities is obvious, although Dr. C. P. Leake of the United States Public Health Service tells us he has seen similar epidemics in other parts of this country. Apparently a mutation of the virus has been effected, with consequent alterations of virulences, affinities and immunogenic properties; although, however, convalescent serum from these patients has been shown in our laboratory to neutralize the Flexner strain of poliomyelitis virus.

A slight outbreak occurred again this year, with pronounced antecedent gastro-intestinal symptoms and, in some cases, atypical residual findings. These included, in addition to the usual pareses of isolated muscle groups and localized tenderness, occasional persistent hyperactive reflexes and, in one case, a persistent clonus. A more than usual incidence of so-called "Spencer's disease," the intractable gastro-enteritis of doubtful etiology, suspiciously due to a filterable virus, is complicating the picture and may be related to this atypical "polio."

Time has furnished us preliminary data on the value of Brodie's and Kolmer's vaccines. Nearly two thousand injections have been given throughout Southern California with no untoward reactions. Apparently there is no hazard, or at least a minimal one, attending its use. Premature reports indicate a much lower incidence of the disease among those immunized than among those not treated. One of our five fatal cases of the medullary type seen this spring had received one injection of five cubic centimeters of the Brodie vaccine one month prior to the onset of symptoms, but, of course, this one case proves nothing. We are maintaining an open-minded attitude, without letting our enthusiasm run rampant, but nevertheless experiencing a feeling of hopeful expectancy.

THE LURE OF MEDICAL HISTORY*

MR. JOHN HUNTER ON GENERATION † ‡

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II**

HUNTER'S OBSCURE LANGUAGE

HUNTER'S failure to express himself clearly has often been commented upon and reminds one of similar comments regarding Harvey's Latin. Both Owen (1840) and Russell (1916) emphasized the use by Hunter of somewhat confused language in connection with the above statement of the theory of recapitulation. Owen wrote: "We may, I think, perceive, from the evident difficulty with which Hunter expresses the idea, that his mind was oppressed with both its novelty and vastness. Men's thoughts require to be familiarized with propositions of such generality before their exact limits and full application can be appreciated." (Preface to *Animal Economy*, p. 26.) Butler (1910), however, thought that Hunter's "... difficulty in the presentation of abstract ideas [was] not wholly attributable to the novelty of his doctrine," and Singer (1928) even said that Hunter

* A Twenty-Five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of CALIFORNIA AND WESTERN MEDICINE. The column is one of the regular features of the Miscellany department, and its page number will be found on the front cover.

† Because John Hunter occupies so large a place in the development of surgery, it is commonly but erroneously assumed that he had the title of Doctor of Medicine.

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** Part I of this paper was printed in the August issue, CALIFORNIA AND WESTERN MEDICINE, page 145.

"... like Leonardo, ... was handicapped at every turn by literary incoherence. ... Fully to appreciate so incoherent a writer, it is unfortunately necessary to wade through many works written in his own clumsy and ill-arranged manner. To gain any real idea of this great personality, we must consult the writings of his contemporary colleagues." (pp. 165-166.) So well-informed an historian of science as Singer undoubtedly is justified in this opinion, but I received a somewhat more favorable impression from my limited reading of Hunter. Moreover, if one could place one's self in the scientific atmosphere of Hunter's time, some passages would lose their apparent obscurity or seeming contradiction. Owen, to be sure, lived near enough to the time of Hunter to be able to do this, and Singer is able to effect the same result through his large knowledge of the history of science. Some of the obscurity in Hunter's writings may, however, have another source; for Hunter, like Harvey, had an aversion against using new words, and said "... to coin words would not answer the purpose, because then I must have a dictionary of my own."

ON SEMEN

Hunter held "... that the semen differs very little from common mucus," and said that it was regarded as the "most balsamic part," though it was "not a bit more 'balsamic' than the parents it sprung from." (*Essays and Observations*, i, p. 193.) He rightly thought that ejaculation of it relaxes and weakens the individual more than does any other discharge, because of the accompanying spasm which, like fainting fits, produces sleep.

Hunter also deserves a great deal of credit for recognizing that the term "vesiculae seminales" really is a misnomer. In his notes on the guinea pig, he wrote: "Supposing I have called the foregoing bags 'vesiculae seminales,' yet I do not believe that they are so for these reasons: first, the mucus that they contain is by much too thick; secondly, it is thickest at the entrance of the ducts, where we would expect to find it thinnest if it were semen; for it would be natural to suppose that the last that came in would be the thinnest; thirdly, it is not natural to suppose that it would be in such quantity as to lie in the urethra; fourthly, it is not at all of the colour of the semen that is in the vasa deferentia, excepting that part that is in the urethra which seems to be mixed with it; fifthly, as that in the urethra is of a different colour (but differs very little in consistence), and that difference is owing to a mixture of semen, that would show that no semen is mixed with the secretion that is within the bags; sixthly, the mucus that is within the bags is the same as that which is within the prostate gland; for they have no prostate, if the glands which I take to be the prostate be not it; seventhly, the vasa deferentia do not open into these bags, nor communicate therewith, excepting by means of the urethra." (*Essays and Observations*, ii, pp. 210-211.)

Under the heading "Observations on the glands situated between the rectum and bladder, called

vesiculæ seminales," he further wrote: "Those bags, in the male of some animals, which are situated between the bladder and rectum, and commonly called 'vesiculæ seminales,' have been considered as reservoirs of the semen secreted by the testicles, in the same manner as the gall-bladder is supposed to be a reservoir of the bile. Physiologists must have been led to form this opinion from observing that in the human subject their ducts communicate with the vasa deferentia before their termination in the urethra. This communication was supposed to allow the semen, when not immediately wanted, to pass into the bags from the vasa deferentia by a species of regurgitation. But more accurate observations respecting their structure and contents in the human subject, and on corresponding parts in other animals supposed to answer a similar purpose, joined to the circumstance of their not being found in every class, induced me to conclude that this opinion was erroneous. To throw as much light upon this subject as possible, I made a number of experiments, and availed myself of every opportunity which offered of examining whatever could in any way elucidate the point; and, from what I have been able to collect, I think it will appear that they cannot be considered as reservoirs of the semen.

"To proceed regularly with my investigation, I shall begin by comparing the contents of these vesiculæ with the semen as it is emitted from the penis of a living man. From which comparison it will appear that the two secretions are very different in their sensible properties of colour and smell; and although the semen which constitutes the first part of the emission is evidently different from the last, yet every part of it is unlike the mucus found in these vesiculæ." (*Animal Economy*, p. 58.)

INFERENCES CONCERNING SEMINAL VESICLES AND SEMEN

"From the facts which I have stated respecting the organs of generation, the observations which I have made, and the series of actions which I have considered as taking place in the copulation of animals, I think the following inferences may be fairly drawn.

"That the bags, called vesiculæ seminales, are not seminal reservoirs, but glands secreting a peculiar mucus; and that the bulb of the urethra is, properly speaking, the receptacle in which the semen is accumulated previous to ejection.

"Although it seems to have been proved that the vesiculæ do not contain the semen, I have not been able to ascertain their particular use; we may, however, be allowed upon the whole to conclude that they are, together with other parts, subservient to the purposes of generation." (*Ibid.*, p. 70.) Although Hunter was mistaken in saying that no spermatozoa are forced into the vesicles, and that the contents of the seminal vesicles do not form a part of semen, or ejaculate, it is regrettable that there still are genito-urinary specialists who are unaware that he, and Thomas Wharton before him, were correct in regard to the major conclusion.

HUNTER'S EFFORTS TO FIND THE MAMMALIAN OVUM

Hunter apparently made repeated attempts to find the mammalian ovum in the ovaries of hogs, sheep, asses and so forth; killing the female a few days after mating. Since he was unaware of the fact that the ova by this time had been discharged from the ovary and probably had undergone maturation and fertilization, or even had entered the uterus, he merely cut into the remaining "ova sacs"—that is, the Graafian follicles—and carefully looked for ova, but found none. He unfortunately did not always give the exact time that elapsed before he killed the female, and seems to have thought that, instead of being of first importance, this was of little consequence. If he ever opened ovaries containing ripe Graafian follicles, he probably did not recognize the ovum because, like all others of his and later times, he probably looked for something larger. This was also the conclusion of Sir Richard Owen, who in a footnote said: "The ovarian ovum, of which Hunter appears to have been in question, being pellucid, colorless, and much more minute than he anticipated, escaped his observation." It is not surprising that this should have been the case, for it had long been known that, in general, the larger the bird or reptile, the larger the egg. Moreover, the eggs of amphibia and fish had long been known and were easily detected, and it was a fair supposition that the eggs of mammals would at least have appreciable size, even if a similar volumetric ratio did not obtain among mammals as among amphibia or birds.

It is puzzling why Hunter did not find a conceptus at the time of autopsy, in the uterus of a young woman who "poisoned herself in the first month of her pregnancy"; for it is explicitly stated that "... no precaution was omitted which could be devised to prevent it being overlooked or destroyed." It is recorded that: "The uterus was opened in a basin of clear water, the incision was conducted with great circumspection, and very slowly continued, till the whole of the cavity was exposed. Every part of the internal surface was minutely examined with magnifying glasses; but in no situation was there anything resembling an embryo to be found.

"The presence of a corpus luteum, the enlargement of the uterus, the newly formed vascular membrane, or decidua, lining the cavity, and the history of the case, sufficiently prove conception to have taken place; and the embryo being nowhere detected by an examination so accurate and conducted by an anatomist so skillful in minute investigations, would induce a belief that the foetus had not been sufficiently advanced to take on a regular form." In a footnote to these words, Owen said that "With respect to the negative results of Mr. Hunter's examination relative to the reception of the foetus in the uterus, and 'its acquisition of a visible form,' I suppose that the word 'foetus' is here used to express the product of generation, or ovum, especially as it is stated, that 'in the examination of the uterus and Fallopian tubes, Mr. Hunter's chief object

was the detection of the "embryo." Now if the product of generation were really expected to have been seen in that state of development which we understand by the terms embryo and foetus, its presence was most likely overlooked; since, from the analogy of the dog and rabbit, it most probably would have existed merely as a small pellucid vesicle or ovum, supposing that it had escaped from the ovarium; and it is to be regretted that the expression 'there was found in the left "ovarium" a corpus luteum' is all the evidence on that point which the present case affords." In an addendum to this footnote, Owen quoted Home as having stated in the Philosophical Transactions, page 255, that "'As the ovum was so extremely small as to admit of dispute whether it was one or not, I carried it immediately to Kew, to Mr. Bauer, who, after examining it, said it looked like the egg of an insect.'" Owen added: "Mr. Clift, who laid open the uterus in question, and patiently scrutinized the whole of its cavity without perceiving any trace of an ovum, has always been of opinion that the one afterwards detected by Home was dropped from one of the numerous flesh-flies which were buzzing about at the time of the examination." (Animal Economy, pp. 91-93.) These words of Owen might imply that Mr. Clift instead of Mr. Hunter made the examination, were it not for the fact that in the footnote mentioned above, Owen spoke of "... the negative results of Mr. Hunter's examination . . ." and Ogle, whose words are amplified by Owen's footnote, spoke of the examination as having been "... so accurate and conducted by an anatomist so skillful in minute investigation. . . ." Since Mr. Clift was a young man of only seventeen or eighteen years, these words could hardly apply to him and we may hence conclude that it was John Hunter himself who had carefully scrutinized the specimen.

HUNTER'S EXPERIMENTAL ATTITUDE

Because Hunter was mainly impressed with the rôle of function and perhaps believed that it was the creator of structure, it is not surprising that he seems to have lacked equal appreciation for minute morphology. Hunter's feeling for function had the great compensation that he realized the value of experiment. Everyone remembers his oft-quoted words to Jenner: "I think your solution is just; but why think? why not try the experiment? Repeat all the experiments upon a hedgehog as soon as you receive this, and they will give you the solution." His experimental attitude is also exemplified very well by his notes of December 24, 1781, in which he stated:

"In a sow which took the boar on Tuesday and was killed the Thursday sennight following, in the morning, which was about ten days after, the glands of the ovarium [ovisacs or Graafian vesicles] were swelled a little, and, when cut into, contained coagulated blood. Some of them contained pieces bigger than a cherry stone, others were less. The horns of the uterus seemed preparing for the ova, being divided into partitions by a tightness of stricture, but of unequal lengths, some being as long again as others; and those

divisions corresponded with the number of glands in one [the ovarium of that] side, being eleven in number; [those of] the other side could not be counted, owing to its being opened later, by which means the parts were not so distinct.

"A sow that had taken the boar, April the —, was killed April —, viz., — days after.

"[The dates are lost; however, it is not material; it shows the progress and difference in the same animal, some being further advanced than others.—J. H.] [*The dates, to be sure, were of crucial importance.*]

"The following appearances were observed: The ovarium of the right side was larger than that of the left. There appeared several ova [ovisacs] that were more vascular and larger than the others. These were eleven in number, each of which had a part projecting like a nipple, which was more evident in some than in others. The remaining number had this appearance beginning to take place; the other ova [ovisacs] were smaller, of a yellowish white, harder and firmer in consistence. When cut into, they appeared of the same colour [throughout] their whole substance.

"One of the eleven [ovisacs] appeared as if it had burst. When cut into, it had an irregular appearance of a cavity, in which there was extravasated coagulated blood. On cutting into the other ova [ovisacs] which seemed impregnated (viz., those which had the projecting appearance), they seemed to be taking on more the appearance of a cavity; which in some of them contained a yellowish serum, in others coagulated blood, but of irregular form, like extravasation into the substance. This was much more in some than in others.

"In the other [ovisacs] that had not the above projection, their cavities appeared more circumscribed and perfect; their inner surfaces were very vascular with partial exudations of coagulated blood, and they contained a serum. The left ovarium had seven of the ova [ovisacs] of a red colour, four of which had a projection. One of them seemed ready to burst; and in cutting into its substance, one cavity, whose surface was vascular, was covered with coagulated blood, and contained also serum. The other three were not so much advanced; but all contained coagulated blood, which might be separated from all sides of the cavity.¹

"In the uterus of a sow sixteen days gone, the foetus was formed, and its purse-shaped membrane [chorion and allantois] was above a foot long in some. This membrane, with the foetus nearly in the middle between each end, occupied nearly the whole length of the cavity of the uterus, like a tape-worm in the intestines. Through the whole course of the uterus was a white mucus

¹[Here the process of examination seems to have been sections across, or cutting into the substance of the ovisac, whereby the true ovum was most probably destroyed, and its contents only observed, which might have been the 'serum' that Hunter mentions. Had the exterior covering of the mammillary eminence been carefully scratched open, the ovarian ovum might have been detected and removed entire.] It would have been better had Sir Richard said that the ovum probably was lost, and it is highly improbable that anyone could have observed its contents without considerable magnification.

almost like cream; and where the foetus lay, this was most in quantity.

"In two other sows that were only allowed to go ten days, I could not observe any change whatever, and there was none of the mucus to be found in either uterus." (Essays and Observations, *i*, pp. 196-198.)

In the "Experiments on Sows" made in December, 1781, and in that on an ass in October 2, 1789, for the purpose of discovering the early ovum, Hunter does not seem to have profited by the important experiments and observations of Cruikshank on rabbits. This is very surprising, for he seems to have been on friendly terms with him, and Cruikshank stated that the results of his work had been incorporated in the lecture on the gravid uterus given annually at the Great Windmill Street school, for nineteen years before their publication in 1797. Von Baer regarded them as so accurate and so suggestive that he wondered why the mammalian ovum had not been discovered before. It would seem that John, like William Hunter and Haighton, did not grasp the import of Cruikshank's findings and hence still sought for the ovum in the ovary ninety-two hours after copulation in the ass, and nine days after copulation in the sow.

The constrictions in the cornua which Hunter noticed do not indicate that the blastocysts had already implanted, for in a personal letter Professor Corner informed me that they do not become fixed until the thirteenth day. He further suggested that the constrictions which Hunter saw were transient muscular contractions. Weyssé stated in 1894 that the largest blastodermic vesicle found by him in the sow before eleven days measured 3.9 millimeters, and that one seen ten days after mating measured only 1.95. According to Assheton (1898), the blastodermic vesicle increases from 0.2 to 1.95 millimeters from the seventh to the ninth day, and is 3.35 millimeters large by the tenth day. According to Corner, the blastocysts of the hog are soft, collapsed vesicles a few millimeters in diameter, nine days after mating, elongation beginning on the eleventh day. There seems to be no agreement among investigators regarding this matter, however, for it has been estimated that they are up to forty millimeters in length at this time. If so, it seems that Hunter would have recognized them. In the ass they probably were still in the tubes, and Hunter hence failed to find anything except the ruptured follicles and corpora rubra in the latter.

ON LOCAL RESPONSE IN GROWTH

It is especially interesting to note that Hunter called attention to the fact that there is a marked local response in growth at the site of uterine implantation. He thought that the human fetus probably moved more than that of any other animal because of the great length of its cord and the presence of a relatively large amount of amniotic fluid. He apparently had a good idea of the gross formation of the yolk or ovum in the ovaries of the fowl, and he seems to have watched the development of the eggs with great

care, though he does not seem to have availed himself of the microscope to any extent. He preferred to speak of the albumen of the egg as slime, and knew that it was produced by the oviduct. He thought that it "... comes nearest to the nature of blood of any animal substance we know; and we know it is alive, therefore not necessary to undergo any change to have this effect produced; for it is only the absorption of living parts, therefore is capable of composing the animal without having undergone the act of digestion. . . ." (Essays and Observations, *i*, p. 202.)

"FUNCTIONS OF NUTRITION AND ABSORPTION"

This is in harmony with his idea that chyle has life, and that food becomes "animalized" during digestion. When considering the "Functions of nutrition and absorption," he also wrote: "The remote cause of absorption of whole and living parts implies the existence of two conditions, the first of which is a consciousness, in the part to be absorbed, of the unfitness or impossibility of remaining under such circumstances, whatever they be, and therefore they become ready for removal, and submit to it with ease. The second is a consciousness of the absorbents of such a state of the parts. Both these concurring, they have nothing to do but to fall to the work." Since Palmer's comment upon this idea of Hunter is so pertinent and so timely even today, I shall insert his words. He wrote: "The reader, I imagine, will scarcely refrain from smiling at the *naïveté* with which our author here ascribes consciousness and intelligence to an animal body, to an extent little inferior to Boerhaave, Van Helmont, or even Stahl. It were devoutly to be wished that the *body politic* possessed a similar consciousness of what ought to be done, and an equal will and power to carry its resolutions into effect." (Principles of Surgery, p. 49.)

It will be recalled that Hunter also looked upon the blood as living and as extraordinarily potent, recalling very much the opinions of Harvey; but it is rather surprising that he held the view that the albumen could be incorporated directly into the body of the developing embryo without digestion, for, as to the yolk, he stated very clearly that as "... this membrane [*"membrana vitelli"*] advances, the yolk becomes fluid, beginning at first where the membranal forms, extending itself as the membrane of the yolk extends, by which means the yolk is rendered fit for passing through the duct into the intestine, after the chick is hatched; and it is even not coagulable with heat, so that we may know when an egg has been sat upon, when boiled, for the yolk remains a thin and watery fluid." (Essays and Observations, pp. 208-209.)

HUNTER'S IDEA OF FERTILIZATION

Hunter's idea of fertilization was akin to Harvey's in that he also believed it was due to an influence; not the influence of the male upon the female, however, but of semen upon the ovum. This conclusion seemed to him to be supported by some experiments upon silkworms, for he said: "In dissecting the female parts in the silk-moth,

I discovered a bag lying on what may be called the vagina, or common oviduct, whose mouth or opening was external, but it had a canal of communication between it and the common oviduct. In dissecting these parts before copulation I found this bag empty, and when I dissected them after, I found it full. Suspecting this to contain the semen of the male, I immediately conceived the following experiment. I opened the female as soon as the male had united to her, and found the penis in the opening of this bag, and by opening the duct where the penis lay I observed the semen lying on the end of the penis. In another, I observed the bag to fill in the time of copulation; and in a pair that died in the act, I found the penis in this passage.

"When we consider the impregnation of the egg in the silk-worm, we may observe the following circumstances:

"First, many of the ova are completely formed, and covered with a hard shell, before copulation; secondly, the animals are a vast while in the act of copulation; and, thirdly, the bags at the anus are filled during the time of copulation. From the first observation it appears that the egg can receive the male influence through the hard or horny part of the shell. To know how far the whole, or only a part of the eggs, were impregnated by each copulation, I made the following experiments. I took a female just emerged out of her cell, and put a male to her, and allowed them to be connected their full time. They were in copulation ten hours. I then put her into a box by herself, and when she laid her eggs, I numbered the different parcels as she laid them, viz., 1, 2, 3, 4, 5; these eggs I preserved, and in the summer following I perceived that the No. 5 was as prolific as the No. 1; so that this one copulation was capable of impregnating the whole brood; and therefore the male influence must go either along the oviduct its whole length, and impregnate the incomplete eggs as well as the complete, which appears to be not likely, or those not yet formed were impregnated from the reservoir in the act of laying: for I conceived that these bags, by containing semen, had a power of impregnating the egg as it passed along to the anus, just as it traversed the mouth of the duct of communication." (Animal Economy, p. 451.)

(To be continued)

CLINICAL NOTES AND CASE REPORTS

EPINEPHRIN BY INHALATION, FOR THE RELIEF OF ATTACKS OF BRONCHIAL ASTHMA

By EDWARD MATZGER, M.D.
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EPINEPHRIN by inhalation, for the relief of the attacks of bronchial asthma, is now a simple procedure, and available to all asthma victims. The technical feat of perfecting an all-glass nebulizer that can actually vaporize watery

solutions has been accomplished. This innovation is of importance both to the patient, who is the victim, and to the physician, who is confronted with the problem of relieving attacks of bronchial asthma.

To those of us who have been of the opinion that the pathology of bronchial asthma is predominantly an edema of the bronchial mucous membrane, epinephrin applied locally appeals as the logical technique for its administration. The ability of the patient to breathe more deeply as the vaporized epinephrin is inhaled through the open mouth, speaks for a progressive shrinking of the edematous bronchial mucous membrane. This ability to shrink edematous bronchial mucous membrane parallels what we can see when epinephrin is applied directly to the swollen nasal mucous membrane.

This idea of inhalation therapy for the relief of bronchial asthma developed shortly after the introduction of the use of epinephrin by injection. I have found references to such attempts in 1921 (Ephraim: Dtsch. Med. Wochenschr.). There are for sale at the present time several motor-driven apparatuses, each said to accomplish vaporization, but I have never found one which truly vaporizes aqueous solutions. Inhalation of epinephrin vaporized by boiling has failed to relieve attacks.

There are several all-glass atomizers on the market which, though they deliver some vapor, also spray droplets. The vapor can be inhaled, but the droplets condense on the buccal and pharyngeal mucous membranes, to the patient's disadvantage. The vaporizer I use holds back the droplets and delivers a considerable quantity of true vapor. A firm* has placed on the market the apparatus of my own design that works satisfactorily.

The epinephrin used must be more concentrated than the usually available 1 to 1,000 strength. I have used epinephrin, distributed by several firms, with satisfactory results, the concentration varying from 1-500 to 1-100 strength. I have checked blood sugars, blood pressures and urine analyses on eight patients, and agree with Dr. K. Lageder, (in the *Beiträge zur Klinik der Tuberkulose*, Vol. 83, page 605,) that there is little or no systemic effect from the small amounts of epinephrin actually absorbed.

It is obvious that epinephrin, five to ten times the strength ordinarily used, should be dispensed only on prescription. I can foresee where patients unusually susceptible to epinephrin might be shocked so severely that death might result. I believe that each patient should be tested for blood pressure changes before, during and after its administration. Should the blood pressure readings indicate a rise unusually high in the systolic pressure, or even as small as a ten to twenty-point rise in the diastolic pressure, this form of therapy might be contraindicated.

I am carrying out a series of detailed studies on hospitalized patients in order to determine the effects as well as the possible dangers. The satis-

* The Vaporizer Products Company, 776 Harrison Street, San Francisco.